SEQUENCE LISTING

<110> James, Kenneth D.
Rahdakrishnan, Balasingham
Malkar, Navdeep B.
Miller, Mark A.
Ekwuribe, Nnochiri N.

<120> NATRIURETIC COMPOUNDS, CONJUGATES, AND USES THEREOF

<130> 014811-205.108

<140> US 10/723,933
<141> 2003-11-26

<150> US 60/429,151
<151> 2002-11-26

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<170> PatentIn version 3.3

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Cys

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Xaa

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Arg Val Leu Arg Arg
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Arg Val Leu Arg
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Ser Ser Ser Ser Gly Leu Gly Cys Xaa
20 25

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Val Leu Arg Arg His
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Val Leu Arg Arg
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Cys Xaa

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20 25 30

Gly Ser Ala Ser Asp Leu Glu Thr Ser Gly Leu Gln Glu Gln Arg Asn
35 40 45

His Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu
50 55 60

Glu Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg
65 70 75 80

Glu Val Ala Thr Glu Gly Ile Arg Gly His Arg Lys Met Val Leu Tyr
85 90 95

Thr Leu Arg Ala Pro Arg Ser Pro Lys Met Val Gln Gly Ser Gly Cys
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Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys
115 120 125

Lys Val Leu Arg Arg His
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Lys Met Val Gln Gly Ser Gly
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Pro Lys Met Val Gln Gly Ser Gly
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Ser Pro Lys Met Val Gln Gly Ser Gly
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Leu His Leu Ala Phe Leu Gly Gly Arg Ser His Pro Leu Gly Ser Pro
20 25 30

Gly Ser Ala Ser Asp Leu Glu Thr Ser Gly Leu Gln Glu Gln Arg Asn
35 40 45

His Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu
50 55 60

Glu Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg
65 70 75 80

Glu Val Ala Thr Glu Gly Ile Arg Gly His Arg Lys Met Val Leu Tyr
85 90 95

Thr Leu Arg Ala Pro Arg Ser Pro Lys Met Val Gln Gly Ser Gly
100 105 110

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Lys Val Leu Arg Arg His
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Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
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Gly Leu Gly Cys Asn Xaa Leu Arg Xaa Tyr
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Asn Val Leu Arg Arg Tyr
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Asn Val Leu Arg Arg
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Asn Ser Phe Arg Tyr

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Arg Ile Lys Met Xaa Ser Xaa Ser Gly Leu Gly Cys
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<223> Xaa may be Arg or Lys

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Xaa Val Leu Arg Xaa
1 5

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<223> Xaa may be Arg or Lys

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<223> Xaa may be Tyr or His

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Xaa Val Leu Arg Xaa Xaa
1 5

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<223> Xaa cannot be Asn if amino acid 25 is Arg and amino acid 26 is Tyr

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<222> (25)..(25)
<223> Xaa cannot be Arg if amino acid 21 is Asn and amino acid 26 is Tyr

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<223> Xaa cannot Tyr if amino acid 21 is Asn and amino acid 25 is Arg

<400> 51

Asp Ser Gly Cys Phe Gly Arg Arg Leu Asp Arg Ile Gly Ser Leu Ser
1 5 10 15

Gly Leu Gly Cys Xaa Val Leu Arg Xaa Xaa
20 25

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<400> 52

Asn Val Leu Arg Arg Tyr
1 5

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<223> Polypeptide may be present or absent

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Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
20 25 30

<210> 54
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<400> 54

Ser Pro Lys Met Val Gln Gly Ser Gly
1 5

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<400> 55

His His His His His His Ala Asp Gly Glu
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<210> 56
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Ala Asp Gly Glu
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<210> 57
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<400> 57

Arg Arg Asp Ala Glu Asp Pro Arg
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<210> 58
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<400> 58

Glu Gly Asp Arg Arg
1 5

<210> 59
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<400> 59

His His His His His His Glu Gly Asp Arg Arg
1 5 10

<210> 60
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<400> 60

Arg Arg Asp Ala Glu Asp Arg Arg
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Arg Gly Asp Ala Glu Asp Pro Arg
1 5

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1 5

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1 5 10

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<400> 65

Ala Arg Gly Asp Ala Glu Asp Pro Arg
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<210> 66
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<400> 66

His His His His His His Xaa Met Met
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Asp Asp Ala Gly Glu
1 5

<210> 68
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Glu Ala Gly Glu
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Glu Gly Asp Ala
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<210> 71
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Glu Gly Asp Ala His His His His His His Glu
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<400> 72

Glu His His His His His His Ala Asp Gly Glu
1 5 10

<210> 73
<211> 32
<212> PRT
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<223> Disulfide bond may be present or absent

<400> 73

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
20 25 30

<210> 74
<211> 32
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<223> Xaa is not Arg

<400> 74

Thr Ala Pro Arg Ser Leu Arg Arg Ser Ser Cys Phe Gly Gly Arg Met
1 5 10 15

Asp Arg Ile Gly Ala Gln Ser Gly Leu Gly Cys Asn Ser Phe Xaa Tyr
20 25 30

<210> 75
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<223> Xaa can be any naturally occurring amino acid

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<400> 75

Ser Pro Xaa Met Met His Xaa Gly Gly Cys Phe Gly Arg Arg Leu Asp
1 5 10 15

Arg Ile Gly Ser Leu Ser Gly Leu Gly Cys Asn Val Leu Arg Xaa Tyr
20 25 30

<210> 76
<211> 38
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<400> 76

Glu Val Xaa Tyr Asp Pro Cys Phe Gly His Xaa Ile Asp Arg Ile Asn
1 5 10 15

His Val Ser Asn Leu Gly Cys Pro Ser Leu Arg Asp Pro Arg Pro Asn
20 25 30

Ala Pro Ser Thr Ser Ala
35

<210> 77
<211> 22
<212> PRT
<213> Homo sapiens

<400> 77

Gly Leu Ser Lys Gly Cys Phe Gly Leu Lys Leu Asp Arg Ile Gly Ser
1 5 10 15

Met Ser Gly Leu Gly Cys
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<210> 78
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<212> PRT
<213> Homo sapiens

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<400> 78

Ser Leu Arg Arg Ser Ser Cys Phe Gly Gly Arg Xaa Asp Arg Ile Gly
1 5 10 15

Ala Gln Ser Gly Leu Gly Cys Asn Ser Phe Arg Tyr
20 25

<210> 79
<211> 17
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<400> 79

Cys Phe Gly Arg Xaa Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly
1 5 10 15

Cys

<210> 80
<211> 36
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<223> Xaa may be any naturally occurring amino acid, and may be present or absent

<400> 80

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Ser Pro Arg Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
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Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Xaa Xaa Xaa Xaa Xaa
            20                  25                  30
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Xaa Xaa Xaa Xaa
35

<210> 81
<211> 6
<212> PRT
<213> Artificial

<220>
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<400> 81

Arg Val Leu Arg Arg His
1 5

<210> 82
<211> 32
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<223> Xaa may be any amino acid other than Lys

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<222> (27)..(27)
<223> Xaa may be any naturally occurring amino acid

<400> 82

Ser Pro Xaa Met Val Gln Gly Ser Gly Cys Phe Gly Arg Xaa Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Val Leu Arg Arg His
20 25 30

<210> 83
<211> 32
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<222> (27)..(27)
<223> Xaa is not Lys

<400> 83

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Xaa Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Val Leu Arg Arg His
20 25 30

<210> 84
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<400> 84

Xaa Cys Phe Gly Arg Arg Met Asp Arg Ile Ser Ser Ser Ser Gly Leu
1 5 10 15

Gly Cys Xaa

<210> 85
<211> 10
<212> PRT
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<400> 85

Ser Pro Lys Met Val Gln Gly Ser Gly Cys

1 5 10

<210> 86
<211> 9
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<400> 86

Pro Lys Met Val Gln Gly Ser Gly Cys
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<210> 87
<211> 8
<212> PRT
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<400> 87

Lys Met Val Gln Gly Ser Gly Cys
1 5

<210> 88
<211> 7
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<400> 88

Met Val Gln Gly Ser Gly Cys
1 5

<210> 89
<211> 6
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<220>
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<400> 89

Val Gln Gly Ser Gly Cys
1 5

<210> 90
<211> 5
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<220>
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<400> 90

Gln Gly Ser Gly Cys
1 5

<210> 91
<211> 4
<212> PRT
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Gly Ser Gly Cys
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<210> 92
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Ser Pro Lys Met
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Ser Pro Lys Met Val
1 5

<210> 94
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Ser Pro Lys Met Val Gln

1 5

<210> 95
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<400> 95

Lys Met Val Gln
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<210> 96
<211> 5
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<400> 96

Lys Met Val Gln Gly
1 5

<210> 97
<211> 6
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Lys Met Val Gln Gly Ser
1 5

<210> 98
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Lys Met Val Gln Gly Ser Gly
1 5

<210> 99
<211> 8
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Lys Met Val Gln Gly Ser Gly Cys
1 5

<210> 100
<211> 6
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<400> 100

Lys Val Leu Arg Arg His
1 5

<210> 101
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<212> PRT
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<400> 101

Lys Val Leu Arg Arg
1 5

<210> 102
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Lys Val Leu Arg
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<210> 103
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<400> 103

Arg Val Leu Arg Arg His

1 5

<210> 104
<211> 5
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<400> 104

Arg Val Leu Arg Arg
1 5

<210> 105
<211> 4
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<400> 105

Arg Val Leu Arg
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<210> 106
<211> 29
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<223> Xaa is not Lys

<400> 106

Ser Pro Xaa Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu
20 25

<210> 107
<211> 26
<212> PRT
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<223> Xaa is not Lys

<400> 107

Ser Pro Xaa Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys
20 25

<210> 108
<211> 33
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<400> 108

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Phe Gly Arg Arg Met
1 5 10 15

Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Arg Val Leu Arg Arg
20 25 30

His

<210> 109
<211> 17
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<223> Xaa can be any naturally occurring amino acid

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<223> Xaa may be Ser or Lys

<220>
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<220>
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<222> (12)..(12)

<223> Xaa is Ser and may be present or absent

<220>
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<223> Xaa is Ser and may be present or absent

<400> 109

Cys Phe Gly Arg Xaa Met Asp Arg Ile Xaa Xaa Xaa Xaa Gly Leu Gly
1 5 10 15

Cys

<210> 110
<211> 32
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<220>
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<220>
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<222> (30)..(30)
<223> Xaa is not Arg

<400> 110

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Arg Xaa Arg His
20 25 30

<210> 111
<211> 32
<212> PRT
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<223> Xaa is not Lys

<400> 111

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Val Leu Arg Arg His
20 25 30

<210> 112
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<223> Xaa may be Lys or Cys

<400> 112

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1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His
20 25 30

Xaa

<210> 113
<211> 26
<212> PRT
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<220>
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<223> Xaa is not Lys

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<223> Xaa may be Gly, Met, Leu, Phe, Ile, or a conservative substitution thereof

<220>
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<222> (24)..(24)
<223> Xaa may be Leu, Trp, Tyr, Phe, or a conservative substitution thereof

<220>
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<222> (25)..(25)
<223> Xaa may be Gly, Arg, or a conservative substitution thereof

<400> 113

Ser Pro Xaa Met Val Gln Gly Ser Gly Cys Phe Gly Arg Xaa Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Xaa Xaa Xaa Cys
20 25

<210> 114
<211> 23
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<220>
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<220>
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<223> Xaa may be Thr, Ala, Arg, His, Pro or Glu

<220>
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<223> Xaa may be Lys, Asn, Arg, Ser, Asp or Pro

<220>
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<223> Methylation if Xaa is Asn

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<222> (17)..(17)
<223> Xaa is not Gly

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<222> (17)..(17)
<223> Xaa may be Orn, Har, p-amidinophenyl Ala, or Ile

<400> 114

Lys Cys Phe Lys Gly Lys Asn Asp Arg Xaa Lys Xaa Gln Ser Gly Leu
1 5 10 15

Xaa Cys Asn Ser Phe Lys Tyr
20

<210> 115
<211> 195
<212> PRT
<213> Artificial

<220>

<223> BNP pro-pentapeptide

<400> 115

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His His His His His His Glu Gly Asp Arg Arg Ser Pro Lys Met Val
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Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser
            20                  25                  30

Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His Arg Arg Asp Ala Glu
        35                  40                  45

Asp Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met
    50                  55                  60

Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg
65                  70                  75                  80

His Arg Arg Asp Ala Glu Asp Ser Pro Lys Met Val Gln Gly Ser Gly
                85                  90                  95

Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly
            100                 105                 110

Cys Lys Val Leu Arg Arg His Arg Arg Asp Ala Glu Asp Ser Pro Lys
        115                 120                 125

Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser
    130                 135                 140

Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His Arg Arg Asp
145                 150                 155                 160

Ala Glu Asp Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg
                165                 170                 175

Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu
            180                 185                 190

Arg Arg His
        195
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<210> 116
<211> 29
<212> PRT
<213> Artificial

<220>
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<223> Xaa may be Lys, Arg, or Gly; must be Lys if amino acids 2 and 26 are not Lys

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<223> Xaa may be Lys, Arg, or Gly; must be Lys if amino acids 2 and 13 are not Lys

<400> 116

Pro Xaa Met Val Gln Gly Ser Gly Cys Phe Gly Arg Xaa Met Asp Arg
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Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Val Leu Arg
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<400> 117

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1 5 10 15

Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Xaa Xaa Xaa Xaa
20 25 30

Xaa Xaa Xaa Xaa Xaa
35

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<400> 118

Gln Gly Ser Gly
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<400> 119

Val Gln Gly Ser Gly
1 5

<210> 120
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<400> 120

Met Val Gln Gly Ser Gly
1 5

<210> 121
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<400> 121

Pro Lys Met Val Gln Gly Ser Gly
1 5

<210> 122
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<400> 122

Ser Pro Lys Met Val Gln Gly Ser Gly
1 5

<210> 123

<211> 29
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<400> 123

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu
20 25

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<400> 124

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys
20 25

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Ser Ser Ser Ser Gly Leu Gly Cys Xaa
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Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile
1 5 10 15

Ser Ser Ser Ser Gly Leu Gly Cys
20

<210> 128
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<400> 128

Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly
1 5 10 15

Cys

<210> 129
<211> 18
<212> PRT
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<220>
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<400> 129

Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly
1 5 10 15

Cys Lys

<210> 130
<211> 23
<212> PRT
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<220>
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<400> 130

Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly
1 5 10 15

Cys Lys Val Leu Arg Arg His
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<400> 131

Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Xaa Met Asp
1 5 10 15

Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Xaa Val Leu Arg Arg His
20 25 30

<210> 132
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Cys Phe Gly Arg Xaa Met Asp Arg Ile Ser Ser Ser Ser Gly Xaa Gly
1 5 10 15

Cys

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Ser Pro Xaa Met Val Gln Gly Ser Gly
1 5

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Xaa Val Leu Arg Arg His
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<400> 135

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1 5 10 15

Arg Ile Gly Leu Gly Cys Xaa Xaa Xaa Xaa Xaa Xaa
20 25

<210> 136
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<400> 136

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1 5 10 15

Asp Arg Ile Xaa Xaa Xaa Xaa Gly Leu Gly Cys Xaa Xaa Xaa Xaa Xaa
20 25 30

Xaa Xaa Xaa Xaa Xaa
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Arg Ile Gly Ser Leu Ser Gly Leu Gly Cys Asn Val Leu Arg Xaa Tyr
20 25 30